

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-24 (canceled)

- A2
- ~~25.~~ (new) An isolated polypeptide containing the amino acid sequence represented by SEQ ID NO:24; or containing (i) an amino acid sequence represented by SEQ ID NO:24, of which one or more amino acids are deleted, (ii) an amino acid sequence represented by SEQ ID NO:24, to which one or more amino acids are added, (iii) an amino acid sequence represented by SEQ ID NO:24, into which one or more amino acids are inserted, (iv) an amino acid sequence represented by SEQ ID NO:24, in which one or more amino acids are substituted by other amino acids, or (v) an amino acid sequence represented by SEQ ID NO:24 containing a combination of the modifications described in the above (i) to (iv), and having a biological activity substantially equivalent to that of the polypeptide having the amino acid sequence shown by SEQ ID NO:24; or its amide or ester; or a salt thereof.
26. (new) The polypeptide, its amide or ester, or a salt thereof, according to claim ~~25~~, which contains the amino acid sequence represented by SEQ ID NO:6; or which contains (i) an amino acid sequence represented by SEQ ID NO:6, of which one or more amino acids are deleted, (ii) an amino acid sequence represented by SEQ ID NO:6, to which one or more amino acids are added, (iii) an amino acid sequence represented by SEQ ID NO:6, into which one or more amino acids are inserted, (iv) an amino acid sequence represented by SEQ ID NO:6, in which one or more amino acids are substituted by other amino acids, or (v) an amino acid sequence represented by SEQ ID NO:6 containing a combination of the modifications described in the above (i) to (iv), and has a biological activity substantially equivalent to that of the polypeptide having the amino acid sequence shown by SEQ ID
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NO:6.

27. (new) The polypeptide or its amide or ester, or a salt thereof, according to claim ~~25~~, which contains the amino acid sequence represented by SEQ ID NO:26.
28. (new) The polypeptide or its amide or ester, or a salt thereof, according to claim ~~26~~, which contains the amino acid sequence represented by SEQ ID NO:12.
29. (new) The polypeptide or its amide or ester, or a salt thereof, according to claim ~~25~~, which contains the amino acid sequence represented by SEQ ID NO:49.
30. (new) The polypeptide or its amide or ester, or a salt thereof, according to claim ~~26~~, which contains the amino acid sequence represented by SEQ ID NO:47.
31. (new) An isolated nucleic acid comprising a nucleic acid having a base sequence encoding the polypeptide according to claim ~~25~~.
32. (new) The isolated nucleic acid according to claim ~~31~~, wherein the base sequence encoding the polypeptide according to claim 1 is the base sequence represented by SEQ ID NO:23.
33. (new) The isolated nucleic acid according to claim ~~31~~, wherein the base sequence encoding the polypeptide according to claim 1 is the base sequence represented by SEQ ID NO:4.
34. (new) The isolated nucleic acid according to claim ~~31~~, wherein the base sequence encoding the polypeptide according to claim 1 is the base sequence represented by SEQ ID NO:25.
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35. (new) The isolated nucleic acid according to claim ~~31~~, wherein the base sequence encoding the polypeptide according to claim 1 is the base sequence represented by SEQ ID NO:10.
36. (new) The isolated nucleic acid according to claim ~~31~~, wherein the base sequence encoding the polypeptide according to claim 1 is the base sequence represented by SEQ ID NO:48.
37. (new) The isolated nucleic acid according to claim ~~31~~, wherein the base sequence encoding the polypeptide according to claim 1 is the base sequence represented by SEQ ID NO:46.
38. (new) A pharmaceutical composition comprising the polypeptide, its amide or ester, or a salt thereof, according to claim ~~1~~ and a pharmaceutical carrier.
39. (new) The polypeptide according to claim ~~1~~, wherein the biological activity comprises one or more of: expression in cartilage tissue, induction of cartilage differentiation, induction of proliferation of a cell in which the polypeptide is expressed, and binding to an antibody which specifically binds to a polypeptide according to SEQ ID NO. 6, 12, 24, 26, 47 and 49.
40. (new) An isolated nucleic acid encoding a polypeptide according to claim ~~39~~.
41. (new) An isolated polypeptide wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO. 6, 12, 24, 26, 47 and 49.
42. (new) A recombinant vector comprising the DNA according to claim ~~31~~.
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43. (new) A transformant transformed with the recombinant vector according to claim ~~42~~.

44. (new) A method for manufacturing the polypeptide or its amide or ester, or a salt thereof, according to claim 1, which comprises culturing a transformant transformed with the recombinant vector comprising a DNA having a base sequence encoding the polypeptide according to claim 1, and producing the polypeptide.
45. (new) A reagent for screening a compound or its salt that promotes or inhibits the activity of the polypeptide or its salt according to claim 1, which comprises the polypeptide, its amide or ester, or a salt thereof, according to claim 1, wherein the polypeptide comprises a label.
46. (new) A kit for screening a compound or its salt that promotes or inhibits the activity of the polypeptide, its amide or ester, or a salt thereof, according to claim 1, comprising the polypeptide or its salt according to claim 1 and a reagent for measuring a biological activity of the polypeptide.
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RESPONSE

Pending Claims

Claims 1-24 are pending, claims 17, 20, 21, and 24 are withdrawn from consideration. Upon entry of the amendment and response, claims 1-24 cancelled without prejudice and claims 25 – 46 are added. Support for the added claims may be found throughout the specification, and claims as originally filed, and at least at page 7, lines 11 – 24, page 13, lines 6 – 16, page 13, line 17 through page 21, line 19, and in the Examples.

Information Disclosure Statement

Applicants submit herewith a supplementary Information Disclosure Statement providing U.S. Patent Application 5,770,366 which is the U.S. patent corresponding to Reference BA previously filed for which an English Abstract was provided.

Objection to the Specification

The Specification is objected to because the abstract is in two paragraphs. Applicants respectfully submit that the objection is moot in view of the above amendment to the specification and respectfully request that the rejection be reconsidered and withdrawn.

Objection to Claim 16

Claim 16 is objected to for being in improper form. Applicants respectfully submit that the rejection is moot in view of the amendment to the claims as the newly added claims do not contain the objected-to language. Accordingly, Applicants respectfully request that the rejection be

reconsidered and withdrawn.

Claims 1-16, 18-19 and 22 –23 Are Rejected Under 35 U.S.C. § 101

Claims 1-16, 18-19 and 22 –23 are rejected under 35 U.S.C. § 101 as being drawn to non-statutory subject matter. Applicants respectfully submit that the rejection is moot in view of the the claims cancellation of the claims and is improper if applied to the newly added claims. The newly added claims recite “isolated polypeptides” or “isolated DNA” and thus do not read over naturally occurring molecules. Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Claims 1-16, 18-19, and 22-23 Are Rejected Under 35 U.S.C. § 112, Second Paragraph

Claims 1-16, 18-19, and 22-23 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinguish the invention.

Applicants respectfully submit that the rejection is moot in view of the the claims cancellation of the claims and is improper if applied to the newly added claims which no longer contain the language objected to by the Examiner. Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Claims 1-16, 18-19, and 22-23 Are Rejected Under 35 U.S.C. § 112, First Paragraph

Claims 1-16, 18-19, and 22-23 are rejected under 35 U.S.C. § 112, first paragraph for lack of enablement. The Examiner states that the specification does provide sufficient enablement for claims which recite nucleic acid sequences “substantially similar” to the recited SEQ ID NOs. but does acknowledge that the specific sequences claimed are enabled. The Examiner also asserts that the pharmaceutical composition claimed is not enabled because there is no disclosure as to

how to effectively use the composition, and a lack of working examples providing evidence which is reasonably predictive that the composition is effective for in vivo use.

Applicants respectfully submit that the rejection is moot as claims 1-16, 18-19, and 22-23 have been cancelled and traverse the rejection if applied to the newly added claims. As added the claims recite the sequences both in terms of structural and functional features. The sequences encompass specifically recited sequences, as well as those with deletions, additions, substitutions, insertions (or a combination of these) provided that such proteins have a biological activity substantially equivalent to the biological activity of the specifically recited sequence, e.g., such as expression in cartilage tissue, ability to induce cartilage differentiation or proliferation of a cell in which the polypeptide is expressed, and ability to bind to an antibody which specifically binds to the specifically recited polypeptides. As such, polypeptides which do not possess such activity do not fall within the scope of the claims.

With regards to the pharmaceutical composition claim, Applicants respectfully submit that a detailed disclosure of how to use the compositions encompassed by the claim is provided in the specification (see, e.g., pages 27-29) and that the Examiner's requirement for a working example is not legally appropriate. Further, given the high homology of the polypeptides to MIA (melanoma inhibitor activity)/CD-RAP (bovine cartilage-derived retinoic acid-sensitive protein) which plays an active role in the formation and maintenance of joints from a physiological aspect (The Journal of Biological Chemistry, 271, 3311-3316, 1996), cited at page 2 of the application, Applicants respectfully submit that the art is not unpredictable with respect to this class of proteins and therefore it would not comprise undue experimentation to make and use the pharmaceutical compositions comprising the polypeptides as recited in the newly added claims.

Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn.

CONCLUSION

Applicants submit that all claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicants' attorney would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney of record.

Respectfully submitted,

Date:

June 20, 2003

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BOS2_321869.1